



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2018-D-2647]

Inborn Errors of Metabolism That Use Dietary Management: Considerations for Optimizing and Standardizing Diet in Clinical Trials for Drug Product Development; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, Department of Health and Human Services (HHS).

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a revised draft guidance for industry entitled “Inborn Errors of Metabolism That Use Dietary Management: Considerations for Optimizing and Standardizing Diet in Clinical Trials for Drug Product Development.” This draft guidance describes FDA’s current recommendations for optimizing and standardizing dietary management in clinical trials for the development of drug products intended to treat inborn errors of metabolism (IEM) when dietary management is a key component of patients’ metabolic control. Optimizing and standardizing dietary management in these patients before they enter clinical trials and during clinical trials is essential to providing an accurate evaluation of the efficacy of new drug products. This guidance revises the draft guidance of the same name issued on July 24, 2018.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*], to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2018-D-2647 for "Inborn Errors of Metabolism That Use Dietary Management: Considerations for Optimizing and Standardizing Diet in Clinical Trials for Drug Product Development." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions,"

publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at:
<https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001

New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002; or the Office of Communication, Outreach, and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Robert Temple, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 6304, Silver Spring, MD 20993, 301-796-1153; or Diane Maloney, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a revised draft guidance for industry entitled “Inborn Errors of Metabolism That Use Dietary Management: Considerations for Optimizing and Standardizing Diet in Clinical Trials for Drug Product Development.” This draft guidance describes FDA’s current recommendations for optimizing and standardizing dietary management in clinical trials for the development of drug products intended to treat IEM when dietary management is a key component of patients’ metabolic control. Optimizing and standardizing dietary management in these patients before they enter into clinical trials and during clinical trials is essential to providing an accurate evaluation of the efficacy of new drug products.

This draft guidance revises the draft guidance of the same name issued on July 24, 2018 (83 FR 35006). FDA considered comments received on the draft guidance and is reissuing the guidance in draft form. Revisions from the previous draft include: (1) clarification that drug products, including both small molecules and biological products, should be studied in conjunction with dietary management for conditions where dietary management is the current

standard of clinical care; (2) clarification that metabolic control may be evaluated by biochemical analytes and clinical assessment as substantiated by current clinical standards of care; (3) clarification that differences in baseline dietary management standards among patients from different countries should be considered and clearly stated in the protocol; and (4) clarification that the most informative design is a randomized, double-blind clinical trial that includes a concurrent control group (approved drug or placebo).

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on "Inborn Errors of Metabolism That Use Dietary Management: Considerations for Optimizing and Standardizing Diet in Clinical Trials for Drug Product Development." It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR part 312 have been approved under OMB Control No. 0910-0014.

III. Electronic Access

Persons with access to the internet may obtain the guidance at either <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs>, <https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances>, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>, or <https://www.regulations.gov>.

Dated: July 6, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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